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Study of Some New 3-Substituted Indolo [2, 3-B] Oxazin-2-Ones as Anti Fungal Agents

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ABSTRACT

3-substituted indolo [2,3-b] oxazin-2-ones (2) have been prepared by refluxing 2-indolone-3-yl –imino alkanoic acid (1) with fused sodium acetate in acetic anhydride. The compounds prepared were screened for their fungicidal activity against *Pyricularia oryzae. Puccinia graminis, Alternaria solani* and *Phytopthora infestans.*

Keywords: 3-Substituted Indolo [2, 3-B] Oxazin-2-Ones, Anti Fungal Agents

INTRODUCTION

Indoles itself have been found to possess a variety of biological activities such as fungicidal[1], bactericidal[2], antiviral[3], herbicidal[4] and pesticidal[5,6] activities.

Oxazinone ring is reported to have associated with antibacterial[7],herbicidal[8] and fungicidal[9] activities.

When indole ring is coupled with other heterocycles the compounds of varied biological activities[10,11] have been formed. In the present investigation the effort has been made to synthesize compounds in which indole ring was fused with oxazinone ring and screened them for anti fungal activity against *Pyricularia oryzae. Puccina graminis, Alternaria solani* and *Phytopthora infestans*.

EXPERIMENTAL

Melting points of all synthesized compounds were determined in open capillary and uncorrected. IR spectra were recorded on Perkin -Elmer Spectrometer in the range 400-4000cm^{-1}. PMR spectra were recorded with TMS as internal standard using DMSO d_6. Purity of the compounds were checked by TLC on Silica gel –G plates with layer thickness of 0.3 mm. All compounds gave satisfactory C, H, N and S elemental analysis.

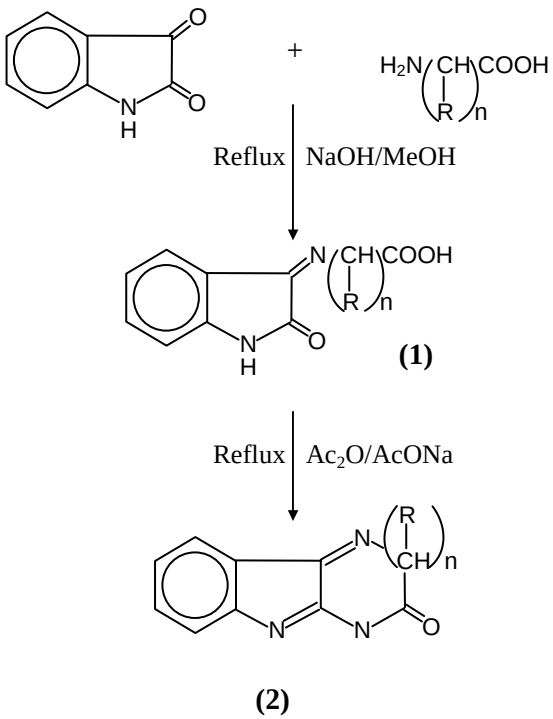
Synthesis of 2-[indolone-3-yl–imino] alkanoic acid (1)

It was prepared by well known method[12]. A mixture of isatin (0.1M), glycin (0.1M) and sodium hydroxide (0.1M) were refluxed in methanol for 4 hours. The solvent was removed and water is poured into the residue to precipitate the desired product which was washed with water dried and recrystallised from ethanol.m.p.180-182^{0}C ; yield 72 %: Significant bands :IR(KBr cm^{-1}) 3475 (NH-Stretching);3208 (OH-Stretching); 1750, 1720 (>C=O-Stretching); 1650 (>C=N -Stretching); 1548, 1518,1508 (Aromatic ring stretching).Other compounds thus prepared are recorded in Table (1).

Synthesis of 3-substituted indolo [2,3-b] oxazin-2-ones (2) (2)

It was prepared by refluxing 2-[indolone-3-yl –imino] alkanoic acid (1) (0.015M) with fused sodium acetate (0.02M) in acetic anhydride for 30 minutes. The solvent was removed and water is poured into the residue to precipitate the desired product which was washed with water dried and recrystallised from ethanol. m.p. 123^{0}C ; yield (50%). Significant bands: IR(KBr cm^{-1}):1745 (>C=O-Stretching); 1620 (>C=N-Stretching); 1545, 1508, 1498 (Aromatic ring stretching); 1288 (C-O-C Stretching); 1097 (C-N-C Stretching): ^{1}HNMR data (DMSO- d_6)δ: 3.3 (s,2H,-NHCH$_2$CO) ;6.4-7.6(m,4H,Ar-H) .Other compounds thus prepared are recorded in Table (1). The synthesis of these compounds has been given in scheme-I.

SCHEME-I



(2)

TABLE (1)

S.No.	R	n	m.p. (^{0}C)	Yield (%)	Molecular Formula	Analysis			
						Carbon (%)		Hydrogen (%)	
						Found	Calc.	Found	Calc.
1a	H	1	182	72	$C_{10}H_8O_3N_2$	59.13	58.82	4.12	3.92
1b	CH_3	1	195	71	$C_{11}H_{10}O_3N_2$	60.99	60.55	4.99	4.59
1c	$CH(CH_3)_2$	1	165	70	$C_{13}H_{14}O_3N_2$	62.81	63.41	5.19	5.69
1d	CH_2OH	1	178	68	$C_{11}H_{10}O_4N_2$	55.97	56.41	4.83	4.27
1e	CH_2SH	1	169	71	$C_{11}H_{10}O_3N_2S$	53.12	52.80	3.79	4.00
1f	CH_2COOH	1	148	70	$C_{12}H_{10}O_5N_2$	55.26	54.96	3.24	3.82
1g	CH_2CH_2COOH	1	157	64	$C_{13}H_{12}O_5N_2$	56.99	56.52	4.81	4.35
1h	CH_2CONH_2	1	164	62	$C_{12}H_{11}O_3N_4$	56.01	55.59	4.92	4.25
1i	$CH_2CH_2CONH_2$	1	143	68	$C_{13}H_{13}O_4N_3$	57.18	56.73	5.11	4.73
1j	CH_2 $CH(CH_2)_2$	1	155	65	$C_{14}H_{14}O_3N_2$	64.83	65.12	5.98	5.43
2a	H	1	123	50	$C_{10}H_6O_2N_2$	65.06	64.52	2.99	3.23
2b	CH_3	1	138	58	$C_{11}H_8O_2N_2$	65.90	66.00	3.76	4.00
2c	$CH(CH_3)_2$	1	129	69	$C_{13}H_{14}O_2N_2$	68.16	67.83	5.93	6.09
2d	CH_2OH	1	141	65	$C_{11}H_8O_3N_2$	60.81	61.11	4.11	3.70
2e	CH_2SH	1	127	63	$C_{11}H_8O_2N_2S$	57.16	56.89	3.96	3.45
2f	CH_2COOH	1	122	65	$C_{12}H_8O_4N_2$	58.72	59.02	2.76	3.08
2g	CH_2CH_2COOH	1	138	58	$C_{13}H_{10}O_4N_2$	59.86	60.46	4.02	3.87
2h	CH_2CONH_2	1	124	54	$C_{12}H_9O_3N_3$	58.99	59.26	3.99	3.70
2i	$CH_2CH_2CONH_2$	1	128	52	$C_{13}H_{13}O_3N_3$	60.85	60.23	4.82	5.02
2j	CH_2 $CH(CH_2)_2$	1	137	51	$C_{14}H_{13}O_2N_2$	70.11	69.71	5.98	5.39

Evaluation of fungicidal activity

The anti fungal activity was evaluated by agarplate technique[11] against *Pyricularia oryzae. Puccina graminis* ,*Alternaria solani* and *Phytopthora infestans*. At concentrations 1000 ppm, 100 ppm and 10 ppm. The number of replications in each case was three. On the basis of growth recorded on 7th day of

incubation the fungicidal activity of test compounds was calculated in terms of present inhibition of mycelial growth using the following formula.

Present inhibition of

$$\text{mycelial growth} = \frac{dc - dt}{dc} \times 100$$

Where

dc = Average diameter growth of the colony in control sets on 7th day of incubation.

dt = Average diameter growth of the colony in treatment set on 7th day of incubation.

Diameter growth = apparent diameter of the colony–diameter of colony of the inoculums.

The percentage inhibitions of various compounds are recorded in table -2.

TABLE (2)

S.No.	Average % inhibition after 7 days											
	Pyricularia oryzae			*Puccinia graminis*			*Alternaria solani*			*Phytophthora infestans*		
	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm	1000 ppm	100 ppm	10 ppm
2a	62	45	26	63	46	27	64	47	28	65	48	29
2b	64	47	27	65	48	28	65	47	28	66	49	30
2c	68	49	29	69	50	29	69	51	29	67	48	27
2d	72	51	31	73	52	32	71	50	30	78	54	35
2e	74	52	32	75	53	33	74	51	31	76	54	34
2f	73	52	31	72	50	30	73	52	31	75	52	32
2g	66	48	28	67	46	26	66	46	26	69	47	29
2h	82	58	34	81	60	32	82	61	36	86	64	37
2i	83	56	36	84	64	34	83	62	37	88	67	38
2j	80	52	31	80	53	32	80	53	32	81	57	34
Carbendazim	100	78	54	100	79	55	100	79	54	100	78	55

RESULTS AND DISCUSSION

It is evident from the activity data that the all of the tested compounds have significant anti fungal activity at 1000 ppm against all the fungi but their toxicity decreased considerably at lower concentration, although compounds having serial number 2d, 2e, 2f, 2g, 2h, 2i and 2j show greater anti fungal activity against all the test species but the result are not very spectacular except for compounds 2h, 2i and 2j. Compounds 2h, 2i and 2j showed anti fungal activity in the range of 80-88 % .

It is also evident from the anti fungal screening data that these compounds

are more active on *P. infestans* in comparison to other test fungal species. It is also observed from the result that introduction of polar substituents like -NH_2 group enhances the fungicidal activity.

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REFERENCES

1. Mitani A. and Saiga M., Jpn Kokai Tokkyo Koho, JP 2647; *Chem. Abstr*., 132, 93313m, (2000).
2. Sengupta A.K., Pandey A.K., Verma H.N. and Khan M.M.A.A.; *Chem. Abstr*., 105, 29429u, (1986).
3. Miller W. H., Newlander K.A. and Seefield M., PCT Int. Appl. W0 0072, 846 (CI, A61K31/437) 2000; *Chem. Abstr*., 134, 29317e, (2001).
4. Max M., Ger. Offen, 2, 500, 490/1975; *Chem. Abstr*., 83, 193293t, (1975).
5. Dorgerloh M., Kretschmer A. and Schmidt R. R. , Ger. Offen, DE 3, 537, 828/1978; *Chem. Abstr*., 107, 54193v, (1987).
6. Piscopo E., Durma M. V. and Inperadice M. F.; *Chem. Abstr*., 105, 57766v, (1986).
7. Sazabo J., *Chem. Heterocycl. Compd*., 15, 291, (1979).
8. Progil Rhone, Ger. Offen, 2, 065, 447/ 1974; *Chem. Abstr*., 80, 83074c, (1974).
9. Schallner Otto, PCT Int. Appl. W0, 0206, 277 (CI. C07D413/ 04), 2000; *Chem. Abstr*., 136, 118455g, (2002).
10. Eslam R. El-Samy, Bassyouni F.A., Abu Bakr S.H., Rady H.M. and Abdlla M.M., *Acta. Pharm*.,60,55-71 (2010)
11. Mandour A.H., Islam R. El-Sawy, Shaker K.H. and Mustafa M.A., *Acta. Pharm.*, 60,73-88 (2010)
12. Nizamuddin , Khan M.H. and Bano Q., *J. Food Agric. Chem.*, 43, 2719, (1995).